PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF TRANSMITTAL
OF COPIES OF TRANSLATION
OF THE INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY
(CHAPTER I OR CHAPTER II
OF THE PATENT COOPERATION TREATY)
(PCT Rules 44*bis*.3(c) and 72.2)

To:

KYOWA HAKKO KOGYO CO., LTD.
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RECEIVED
MAR. 30. 2006
I.P. DEPT

Date of mailing *(day/month/year)* 09 March 2006 (09.03.2006)	
Applicant's or agent's file reference 1562	**IMPORTANT NOTIFICATION**
International application No. PCT/JP2004/005503	International filing date *(day/month/year)* 16 April 2004 (16.04.2004)
Applicant KYOWA HAKKO KOGYO CO., LTD. et al	

1. **Transmittal of the translation to the applicant.**

☑ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).

☐ The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

2. **Transmittal of the copy of the translation to the designated or elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

3. **Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Yoshiko Kuwahara
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 90 90

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference 1562	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2004/005503	International filing date *(day/month/year)* 16 April 2004 (16.04.2004)	Priority date *(day/month/year)* 18 April 2003 (18.04.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant KYOWA HAKKO KOGYO CO., LTD.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 02 March 2006 (02.03.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Yoshiko Kuwahara Telephone No. +41 22 338 90 90

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

Translation

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference 1562	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/005503	16.04.2004	18.04.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant
KYOWA HAKKO KOGYO CO., LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/005503

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☐ in computer readable form

   c. time of filing/furnishing

   ☐ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/005503

Box No. III **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 39

because:

☒ the said international application, or the said claims Nos. 39
relate to the following subject matter which does not require an international preliminary examination (*specify*):

The invention of claim 39 relates to a method of therapy for the human body.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 39

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/005503

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

It appears that the matter common to nerve degeneration drugs containing as the active ingredient the compounds having specific structures represented by the formulae (I) to (V) as set forth in claims 1 to 41 resided in "a nerve degeneration drug containing as the active ingredient a substance inhibiting the activity of a glycogen synthase kinase-3".

On the other hand, a nerve degeneration drug containing a substance inhibiting the activity of a glycogen synthase kinase-3 as the active ingredient is reported in the following document. Thus, the constitution of the above common matter cannot be considered as being novel and, therefore, cannot be regarded as the gist of the invention.

Such being the case, the nerve degeneration drugs containing as the active ingredient the compounds represented by the five different formulae as set forth in claims 1 to 41 cannot be regarded as a group of inventions so linked as to form a single general inventive concept.

Document: WO 02/062387 A1 (SMITHKLINE BEECHAM P.L.C.) 2002.08.15

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☒ all parts

   ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/005503

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	7, 8, 13-15, 17-19, 24, 25, 30-32, 34-38	YES
	Claims	1-6, 9-12, 16, 20-23, 26-29, 33, 40, 41	NO
Inventive step (IS)	Claims		YES
	Claims	1-38, 40, 41	NO
Industrial applicability (IA)	Claims	1-38, 40, 41	YES
	Claims		NO

2. Citations and explanations:

Document 1: WO 02/062387 A1 (SMITHKLINE BEECHAM P.L.C.) 15 August 2002
Document 2: WO 99/42100 A1 (Sagami Chemical Research Center) 26 August 1999 & EP 1057484 A1
Document 3: JP 2-306974 A (Goedecke AG) 20 December 1990 & EP 397060 A3
Document 4: WO 01/13916 (Sagami Chemical Research Center) 01 March 2001 & EP 1224932 A1
Document 5: JP 7-508268 A (Goedecke AG) 14 September 1995 & US 5883114 A
Document 6: WO 00/38675 A1 (SMITHKLINE BEECHAM P.L.C) 06 July 2000
Document 7: LOAST, Maryse *et al.*, Paullones are potent inhibitors of glycogen synthase kinase-3β and cyclin-dependent kinase 5/p25, Eur. J. Biochem., 2000, Vol. 267, pp5983-5994
Document 8: WO 37819 A2 (CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIIQUE) 31 May 2001
Document 9: CHEN, Guang *et al.*, Enhancement of hippocampal neurogenesis by lithium, Journal of Neurochemistry, 2000, Vol. 75, pp1729-1734

Novelty and Inventive Step
Claims 1-3, 20, 37, 38, 40, and 41

Document 1 describes a nerve regeneration drug with a GSK3 antagonist as an active ingredient and describes the possibility of therapy for a variety of nerve diseases with this nerve regeneration drug.

Consequently, the inventions of claims 1-3, 20, 37, 38, 40, and 41 do not appear to be novel or to involve an inventive step.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of V:

Claims 1-3, 5-7, 20, 22-24, 37, 38, 40, and 41

Documents 2, 3 describe use of a compound corresponding to formula (I) in therapy of neurodegenerative diseases.

Consequently, the inventions of claims 1-3, 5-7, 20, 22-24, 37, 38, 40, and 41 do not appear to be novel or to involve an inventive step based on document 2.

Claims 1-3, 5, 6, 8, 10, 20, 22, 23, 25, 27, 37, 38, 40, and 41

Document 4 describes use of a compound corresponding to formula (II) to regulate cell death in diseases such as Alzheimer's disease.

Consequently, the inventions of claims 1-3, 5, 6, 8, 10, 20, 22, 23, 25, 27, 37, 38, 40, and 41 are lacking in novelty and inventive step based on document 4.

Claims 1-3, 5, 6, 20, 22, 23, 37, 38, 40, and 41

Document 5 describes use of a compound corresponding to formula (III) in therapy of neurodegenerative diseases.

Consequently, the inventions of claims 1-3, 5, 6, 20, 22, 23, 37, 38, 40, and 41 do not appear to be novel or to involve an inventive step based on document 5.

Claims 1-3, 5, 9, 10, 20, 22, 26, 27, 37, 38, 40, and 41

Document 6 describes a therapeutic agent for neurodegenerative diseases with a GSK3 antagonist as an active ingredient corresponding to formula (IIIa).

Consequently, the inventions of claims 1-3, 5, 9, 10, 20, 22, 26, 27, 37, 38, 40, and 41 do not appear to be novel or to involve an inventive step based on document 6.

Claims 1-3, 5, 11-15, 20, 22, 28-32, 37, 38, 40, and 41

Document 7 describes a therapeutic agent for neurodegenerative diseases with a GSK3 antagonist as an active ingredient corresponding to formula (IV).

Consequently, the inventions of claims 1-3, 5, 11-15, 20, 22, 28-32, 37, 38, 40, and 41 are lacking in novelty and inventive step based on document 7.

Claims 1-3, 16-20, 33-38, 40, and 41

Document 8 describes utility of a compound that is a GSK3 antagonist with formula (V) in therapy neurodegenerative diseases such as Alzheimer's disease.

Consequently, the inventions of claims 1-3, 16-20, 33-38, 40, and 41 do not appear to be novel or to involve an inventive step based on document 8.

Supplemental Box
Continuation of V:

Claims 1-4, 20, 21, 37, 38, 40, and 41

Document 9 describes a GSK3 antagonist lithium compound that promotes nerve regeneration.

Consequently, the inventions of claims 1-4, 20, 21, 37, 38, 40, and 41 do not appear to be novel or to involve an inventive step based on document 9.

Inventive Step

Claims 1-38, 40, and 41

Because documents 1, 9 describe the use of a GSK3 antagonist as a nerve regeneration drug, the use of another GSK antagonist in place of a compound specifically disclosed in this document could be easily conceived of by a person skilled in the art.

Consequently, the inventions of claims 1-38, 40, and 41do not appear to involve an inventive step based on documents 1-9.